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February 1, 2011

Certified Mail, Return Receipt Requested
Mr. Greg Stein
Ohio Department of Health
Health Assessment Section
246 North High Street
Columbus, OH 43215

Re: Scientific critique of ATSDR's November 9, 2010 Health Consultation for East Liverpool Air Quality – East Liverpool, Ohio

Dear Mr. Stein:

Enclosed for inclusion in your agency's record for the S.H. Bell Company's East Liverpool, Ohio facilities is Gradient Corporation's January 26, 2011 Evaluation of Manganese in Ambient Air in the Vicinity of the S.H. Bell facility in East Liverpool, Ohio. S.H. Bell Company commissioned this report out of a strong concern that ATSDR's November 9, 2010 Health Consultation for East Liverpool Air Quality – East Liverpool, Ohio did not evaluate the complete set of current ambient air data, inappropriately used short term ambient concentrations in evaluating long term exposure, and did not evaluate a number of current peer reviewed literature regarding the long term exposure to manganese, among other things. Gradient concludes that ATSDR's call for evaluation of the health impact of manganese in the region is not scientifically justified.

Please ensure that Gradient's January 26, 2011 Report is included in the official agency record for this facility.

Sincerely,

Scott R. Dismukes

cc: John Bell
Rusty Davis
John Bedeck
Chris Dunay

Evaluation of Manganese in Ambient Air in the Vicinity of the S.H. Bell Company in East Liverpool, Ohio

Prepared for
S.H. Bell Company
2217 Michigan Avenue
East Liverpool, Ohio 43920

January 26, 2011

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Executive Summary

I have been asked to evaluate the Agency for Toxic Substances and Disease Registry's (ATSDR's) Health Consultation (HC) for East Liverpool, Ohio regarding possible human health risks from manganese (Mn) in outdoor air (ATSDR, 2010)[1]. Based on an analysis of the most recent toxicity and epidemiology information for Mn[2], and considering the estimated[3] respirable fraction of the annual average Mn concentrations from multiple years of data, I conclude that Mn in ambient air does not present a toxicological concern for individuals in the East Liverpool community. Thus, the HC recommendation to evaluate "incidence of neurodegenerative diseases in the East Liverpool community…as an indicator of health impacts from exposure to manganese" is not scientifically justified. The bases for my conclusion are as follows:

- The HC conclusions are based on total suspended particulate (TSP) Mn and should instead be based on respirable Mn data. Respirable Mn data are most appropriate for evaluating health effects, since this is the size fraction that deposits within the lungs and because Mn inhalation toxicity values are based on respirable Mn.
- The HC conclusions are based on daily maximums, in addition to monthly and annual average Mn concentrations. Interpretation of chronic toxicity criteria, such as the MRL or the RfC, should be based on annual average concentrations, not daily or monthly concentrations, since such values are intended to be applied to long-term exposures (one year or more).
- The HC does not use the most recent toxicity and epidemiology information from peer-reviewed literature to analyze potential risks from Mn in the East Liverpool ambient air.
- Proposed revisions to the Mn inhalation toxicity value are likely to result in a value higher than the current value, that is still health protective.
- Recent studies support that there is a threshold of 10 $\mu g/m^3$ respirable Mn in air that applies to all age groups including adults, children, neonates, and fetuses (*i.e.*, a chronic long-term inhalable exposure concentration below which Mn brain concentrations do not increase).
- A more scientifically sound evaluation of potential health risks from Mn in East Liverpool ambient air should consider:
  - ▸ Recent epidemiology and toxicology data for Mn inhalation
  - ▸ More recent draft and proposed Mn inhalation toxicity values

[1] I note no opportunity was provided to the public for formal comments on a draft.
[2] Note that Mn is not considered a human carcinogen by US EPA (1993).
[3] As discussed in more detail in Section 2.2 and Appendix A, the respirable concentration of Mn was estimated from the ratio of the inhalable particulate matter Mn (PM_{10}) concentration to the total suspended particulate (TSP) Mn concentration from the Water Plant monitoring station (January – March 2009 data), and is more appropriate for evaluating health risks. PM_{10} = particulate matter with diameter of less than or equal to 10 microns, whereas TSP includes airborne particles of all sizes.

- The proposed threshold for Mn inhalation with respect to increase of Mn brain concentrations
- Estimated (or measured) respirable Mn concentrations as opposed to TSP Mn data for the East Liverpool community
- Annual average, respirable Mn concentrations using data from multiple years as opposed to daily and monthly averages

- Based on the above, I conclude that Mn in ambient air does not present a toxicological concern for individuals living in the East Liverpool community. Moreover, it should be noted that such Mn concentrations likely originate from multiple sources.
- Therefore, there is no sound scientific basis for ATSDR's recommendation to evaluate "incidence of neurodegenerative diseases in the East Liverpool community…as an indicator of health impacts from exposure to manganese."

1 Overview

The Agency of Toxic Substances and Disease Registry (ATSDR) prepared a Health Consultation (HC) to address potential health implications from particulate manganese (Mn) in the ambient air in East Liverpool, Ohio (ATSDR, 2010). The HC summarizes TSP Mn data collected by the Ohio Environmental Protection Agency (OEPA) over the last 10 years from three air monitoring stations in the East Liverpool community (Water Plant, Port Authority, and Maryland Ave). The HC also compares these data to current Mn inhalation reference concentration (RfC) from US EPA (1993) and seeks to evaluate potential health risks from Mn in ambient air. Note that Mn is not considered a human carcinogen by US EPA (1993). I have been asked to comment on ATSDR's analysis and interpretation of the data in regard to potential health effects, if any, from Mn in East Liverpool ambient air.

Based on the material presented in this report, I conclude that Mn in ambient air does not present a toxicological concern for individuals living in the East Liverpool community. Therefore, ATSDR's recommendation to evaluate "incidence of neurodegenerative diseases in the East Liverpool community…as an indicator of health impacts from exposure to manganese" is not scientifically justified.

1.1 Credentials for Dr. Barbara D. Beck

I am a board-certified toxicologist specializing in human health risk assessment. I am a Visiting Scientist in the Department of Environmental Health at the Harvard School of Public Health and a Principal at Gradient, an environmental consulting company that specializes in the fate and transport of chemicals in the environment and human health risk assessment. I am a diplomate of the American Board of Toxicology and a fellow of the Academy of Toxicological Sciences, an organization of which I was president from 2009 – 2010.

With respect to manganese, I have conducted human health risk assessments on Mn and provided the findings to government agencies, including the Michigan Department of Environmental Quality and the New Mexico Environment Department. I have also published peer-reviewed articles on the toxicology of inhaled Mn. I was an appointed member of the scientific advisory committee to the Manganese Health Research Program (MnHRP) (a non-profit research organization, jointly sponsored by the manganese industry and the US Department of Defense) from 2004 to 2008. This committee consisted of scientists from both academia and industry with expertise in neurotoxicology, biostatistics,

risk assessment and other technical disciplines. The mission of the MnHRP was to identify the present state of knowledge on manganese with regard to health studies, risk assessment, and research needs, and to oversee research concerning those needs. My resume is provided in Appendix B.

My higher education began with an A.B. degree (*cum laude*) in Biology from Bryn Mawr College in 1968 and then a Ph.D. in Molecular Biology and Microbiology from Tufts University in 1975. Thereafter, I received postdoctoral training at the University of Massachusetts Medical School and Harvard University, under sponsorship from a Cystic Fibrosis Fellowship and an American Cancer Society Fellowship. During that time, I conducted basic research in molecular biology and in biochemistry. Following my fellowships, I was an instructor in Protein Chemistry at Tufts University School of Medicine between 1978 and 1979, where I researched mechanisms of susceptibility to bacterial infection.

Following Tufts University, I was a research associate from 1979 to 1985 in Respiratory Biology in the Department of Environmental Health at the Harvard School of Public Health. While at Harvard, I developed a short-term bioassay to predict the toxicity of particulate matter and gases for the lungs. This widely accepted technique continues to be used today in the field of pulmonary toxicology. During this time, I was also a fellow in the Interdisciplinary Program in Health at Harvard. As part of this program, I co-authored and edited a monograph on Variations in Susceptibility to Inhaled Pollutants.

Thereafter, from 1985 to 1987, I worked at US EPA as a Regional Expert in Toxicology in Region I, which covers all the New England states. In this capacity, I provided expert advice on multiple matters regarding toxicology, in particular as it pertains to air toxics and soil contaminants. For example, I provided responses to questions on inhalation toxicology from the public, evaluated air impacts of remedial activities at Superfund sites, organized a workshop on the health effects of the air pollutant, ozone, helped prepare a risk assessment for trichloroethylene in air, and developed health-based criteria for lead in soil.

In 1987, I joined Gradient, an environmental consulting firm specializing in human health and ecological risk assessment for chemicals in the workplace, consumer products and the environment for both private and public sector clients, where my position is that of Principal and Director of Health Sciences. My consulting practice at Gradient consists of health risk assessments for cancer and non-cancer endpoints, review of animal toxicology and human epidemiology studies, multi-media assessment of exposure to environmental chemicals, and evaluation of the historical development of toxicology, with

a special emphasis on metals, inhaled chemicals, and complex organic compounds. I continue my relationship with the Harvard School of Public Health to this day, where I have given lectures on ozone toxicology, arsenic risk assessment, and have directed a group project in the Environmental Health course. I have also taught the toxicology section of the Harvard Center for Risk Analysis course "Analyzing Risk: Assessment and Management."

I have served in an advisory capacity to a wide range of governmental and non-profit institutions on issues relating to toxicology, risk assessment and public health. These have included the American Water Works Association Research Foundation Peer Review Panel on Arsenic, the Arsenic Task Force of the Society for Environmental Geochemistry and Health, the Advisory Committee to US EPA on Metal Bioavailability and the National Academy of Sciences. I am also an appointed member of the Board of Health in Watertown, MA, the community in which I reside, and was chair of the board for a number of years. In this capacity, I provide advice on a broad range of public health topics from food safety to evaluation of chemical hazards. I have also provided expert toxicological testimony in legal proceedings.

I have been active in the Society of Toxicology (SOT) for many years. I was president of the New England Chapter of SOT, a member of the SOT Program Committee, and a member of the SOT Continuing Education Committee. I was an appointed member to the Risk Assessment Task Force and an elected member to the Membership Committee. I have organized several workshops at annual SOT meetings.

I have published articles on toxicology and risk assessment in peer-reviewed journals, books, and meeting proceedings, including a proposed reference concentration (RfC) for Mn. These publications have addressed a range of topics, such as improving the scientific basis of risk assessment for chemical mixtures and the use of toxicology in the regulatory process. I have numerous publications regarding inhalation toxicology and metals toxicology. I have also been a peer reviewer for several journals, including *Environmental Research*, *Fundamental and Applied Toxicology*, the *Journal of the Society of Environmental Geochemistry and Health*, and *Environmental Health Perspectives*. I am also on the editorial board of *Human and Experimental Toxicology* and an associate editor for *Toxicology and Applied Pharmacology*.

1.2 Objectives of Analysis

I have been asked to evaluate and comment on ATSDR's HC of ambient air quality in East Liverpool, Ohio (ATSDR, 2010). My evaluation consists of the following:

- I reviewed ATSDR's evaluation of the Mn air data and their conclusions regarding potential human health risk, identifying several scientific concerns with their methodology and conclusions.
- I then conducted an independent evaluation of the Mn air data with respect to human health risk. The specific aims of my analysis with respect to the HC were to:
  - Evaluate information regarding concentrations of Mn in ambient air in East Liverpool
  - Evaluate potential exposures to these concentrations
  - Evaluate the toxicological basis of US EPA's Mn RfC, with respect to how the RfC is applied to the East Liverpool data
  - Review recent epidemiological and toxicological studies for Mn and their potential implications for a reassessment of the Mn RfC
  - Determine whether exposures to Mn in ambient air in the East Liverpool community are toxicologically significant, and present a health risk to the community

Both my comments and conclusions on the HC and my independent analysis of the data are described in the next section.

2 Evaluation of Potential Health Risks from Mn in Ambient Air in East Liverpool, Ohio

This section summarizes and evaluates ATSDR's evaluation of the East Liverpool Mn ambient air data, discussing scientific concerns with the analysis and resulting conclusions and recommendations, followed by my own analysis of the East Liverpool data.

2.1 ATSDR's evaluation of the East Liverpool data does not employ the most reliable methodology to characterize exposure and does not reflect the most current understanding of Mn toxicity

The HC (ATSDR, 2010) evaluated potential health implications from TSP Mn data collected from 1999-2009 from the three air monitoring stations in the East Liverpool community by comparing average daily, monthly, and annual TSP Mn concentrations to the current US EPA Mn RfC (0.05 $\mu g/m^3$) and ATSDR Mn inhalation minimal risk level (MRL) (0.04 $\mu g/m^3$) (US EPA, 1993; ATSDR 2000).

As discussed in the following sections, ATSDR's analysis is not based on the most relevant exposure information for Mn and does not adequately consider current toxicological and epidemiological findings on Mn. Thus, the risks presented are overestimated and the recommendation for health studies in the community is not scientifically supported. Specifically:

- ATSDR did not adequately account for the presence of both respirable and non-respirable Mn in the dataset. Use of the less toxicologically relevant non-respirable Mn data for evaluation of the health significance of Mn in air will yield an overestimate of potential risks as compared to use of data from respirable Mn.
- ATSDR overemphasized the value of average daily and monthly Mn concentrations in their interpretation of Mn air data and did not sufficiently consider the long-term average concentrations of the complete dataset, a dataset which spans over 10 years, and provides a more sound basis for evaluating potential long-term effects of Mn exposure.
- ATSDR (2008) developed a draft Mn MRL of 0.3 $\mu g/m^3$ (7.5-fold higher than the current value, but still health-protective) based on more current information on Mn toxicity; however, the HC (ATSDR, 2010) did not consider this value in developing conclusions regarding potential health risks in the East Liverpool community.
- The HC did not have the benefit of external peer-review, an important tool for ensuring the technical quality of a scientific analysis.

Based on the above concerns, the recommendation by ATSDR to evaluate "incidence of neurodegenerative diseases in the East Liverpool community...as an indicator of health impacts from exposure to manganese" is not scientifically justified. Instead, by using a more reliable Mn exposure characterization and consideration of recent toxicological and epidemiology information regarding Mn, I conclude that exposures to Mn in ambient air does not present a toxicological concern for individuals living in the East Liverpool community.

Further, background concentrations of Mn in the East Liverpool air can range from 0.03 to 6.2 µg/m3 (24-hr average basis), based on examination of Water Plant monitoring station monitoring and meteorological data from 2006 through September 2010 (OEPA, E. Liverpool Heavy Metals TSP Data, 2006 - 2010). The ATSDR HC does not discuss the concentrations in the East Liverpool air in the context of background concentrations. Without adequate analysis of background concentrations of Mn in this community, the HC inappropriately focuses on S.H. Bell Company as a potential source.

2.1.1 Respirable Mn data, as opposed to TSP data, represent the appropriate metric for evaluation of potential human health risk

The average monthly TSP Mn concentrations presented in the HC (ATSDR, 2010) ranged from: 0.1-6.8 µg/m^3 at the Water Plant monitoring station (average of 1.3 µg/m^3); 0.01-1.0µg/m^3 at the Maryland Ave monitoring station (average of 0.18 µg/m^3); and 0.02-1.9 µg/m^3 at the Port Authority monitoring station (average of 0.26 µg/m^3). Note that these ranges are not properly reflected in Table 1 of the main HC report. The Water Plant range is correct; however, ATSDR reports the range for Port Authority as Maryland Ave, and *vice versa*, in this table. The HC did present annual average TSP Mn concentrations (from 1999 – 2009) in Appendix B, but as discussed further below, TSP data include all airborne particles, regardless of size. As shown, the annual average TSP concentrations range from: 0.65-2.48 µg/m^3 for the Water Plant monitoring station; 0.22-0.67 µg/m^3 for the Port Authority monitoring station; and 0.08-0.68 µg/m^3 for the Maryland Ave monitoring station.

TSP data include all airborne particles, regardless of size. Respirable particulate Mn particles are more biologically relevant than TSP Mn particles because respirable Mn particles are capable of penetrating the lung tissue, while larger particles are trapped in the nasal and pharyngeal passages, do not penetrate the lung tissue, and do not enter the circulation (Klaassen, 2008). In addition, the current US EPA Mn RfC and ATSDR MRL are based on respirable Mn concentrations (from the Roels *et al.* 1992 study) and should therefore be compared to respirable Mn data for evaluating potential health risk. The

HC does not contain data on the respirable particulate fraction. In fact, the type of air monitor maintained by OEPA to measure TSP (high-volume monitors), and referenced by ATSDR, does not characterize the various size fractions, and therefore does not allow for measurements of respirable particulate concentrations.

> The ATSDR HC (ATSDR, 2010) makes several statements regarding particle size:
>
> "It should be noted that the MRL and RfC values are based on the respirable fraction of manganese-containing particulates (less than 10 microns in aerodynamic diameter). Although limited follow-up analysis of the TSP filters indicates that a significant portion of the particulates are in the respirable fraction, these concentrations are not directly comparable. However, estimates of the manganese concentration in the respirable fraction significantly exceed the health-based values." (p. 11)
>
> "The occupational study that is the basis of the MRL and RfC evaluated exposure for manganese particles less than 5 microns. These particle sizes are considered to be the 'respirable fraction', which are travel past the nose and upper respiratory system to enter the lungs. The manganese air measurements collected in East Liverpool are total suspended particulate matter. Initial characterization of particles on the TSP filters from East Liverpool indicates an aerodynamic particle size range of 4.4-24.3 microns." (p. 12)

There are no citations or further discussion of the particle size data in the HC, and no basis is provided for the statement that "estimates of the Mn concentrations in the respirable fraction significantly exceed the health-based value." (p. 11) Given that the respirable particulate sizes are 5 microns or less, and the size range presented exceeds the respirable fraction, a careful evaluation and presentation of the sizes of the particles in the TSP is warranted. Unless respirable data are used for comparison to Mn inhalation toxicity criteria, drawing conclusions about potential health risks based on TSP Mn is not scientifically justified. As discussed in Section 2.2, data developed by OEPA for the East Liverpool area are available regarding size fractions of ambient particulate Mn which provide evidence that use of TSP Mn leads to an overestimate of risk. These data are derived from the PM_{10} (particulate matter with size ranging mostly 10 microns or less)[4] sampler maintained by OEPA at the Water Plant Monitoring Station, which began operation in January 2009, but such data was not relied upon by ATSDR in the HC.

2.1.2 Annual average values represent the appropriate averaging time for comparison of ambient data to the RfC and MRL

Since the RfC and MRL are chronic toxicity values (*i.e.*, based on an exposure duration of 24 hours/day for a lifetime of 70 years), these values are intended to be compared to an average

[4] Note that PM_{10} is generally a more conservative estimate of the concentration in the respirable fraction than PM_5.